Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Currently Amended) A method for ~~the detection of~~ detecting the methylation status of a nucleotide at a predetermined position in a nucleic acid molecule comprising ~~the steps of~~

(a) treating a sample comprising said nucleic acid molecule or consisting of said nucleic acid molecule in an aqueous solution with an agent suitable for the conversion of said nucleotide if present in

(i) methylated form; or

(ii) non-methylated form

to pair with a nucleotide normally not pairing with said nucleotide prior to conversion;

(b) amplifying said nucleic acid molecule treated with said agent;

(c) real-time sequencing said amplified nucleic acid molecule; and

(d) detecting whether said nucleotide is methylated or not methylated ~~in~~ at said predetermined position in the sample.

2. (Original) The method of claim 1 wherein said sample is derived from a tissue, a body fluid or stool.

3. (Original) The method of claim 2 wherein said tissue is a tumor tissue, neurodegenerative tissue or a tissue affected with another neurological disorder.

4. (Previously Presented) The method of claim 1 wherein said nucleic acid molecule is a DNA molecule or an RNA molecule.

5. (Currently Amended) The method of claim 1 wherein ~~the amplification in step~~ in (b) the nucleic acid molecule is ~~effected by~~ amplified via LCR or PCR.

6. (Original) The method of claim 5 wherein one amplification primer is detectably labeled.

7. (Currently Amended) The method of claim 6 wherein said ~~label~~ amplification primer is labeled with (a) biotin, (b) avidin, (c) streptavidin or (d) a derivative of (a), (b or (c) or a magnetic bead.

8. (Previously Presented) The method of claim 1 wherein said methylated nucleotide is an adenine, guanine or a cytosine.

9. (Currently Amended) The method of claim 1 wherein said real-time sequencing comprises:

(a) hybridization of a sequencing primer to said amplified nucleic acid molecule in single-stranded form;

(b) addition of a DNA polymerase, a ATP sulfurylase, a luciferase, an apyrase, adenosine-phosophosulfate (APS) and luciferin;

(c) sequential addition of all four different dNTPs;

(d) detection of a luminescent signal wherein ~~the~~ an intensity of

the luminescent signal is correlated with the incorporation of a specific nucleotide at a specific position in the nucleic acid molecule and wherein the intensity of said signal is indicative of the methylation status of said nucleotide ~~in~~ at said predetermined position.

10. (Previously Presented) The method of claim 1 further comprising quantifying the methylated nucleotides.

11. (Previously Presented) The method of claim 1 wherein said agent suitable for the conversion of said nucleotide to pair with nucleotide normally not pairing with said nucleotide is a bisulfite, preferably sodium bifulfite.

12. (Currently Amended) A method for the diagnosis of a pathological condition or the predisposition for a pathological condition comprising detection of the methylation status of a nucleotide at a predetermined position in a nucleic acid molecule comprising ~~the steps of~~

(a) treating a sample comprising said nucleic acid molecule or consisting of said nucleic acid molecule in an aqueous solution with an agent suitable for the conversion of said nucleotide if present in

(i) methylated form; or

(ii) non-methylated form

to pair with a nucleotide normally not pairing with a said nucleotide prior to conversion;

(b) amplifying said nucleic acid molecule treated with said agent;

(c) real-time sequencing said amplified nucleic acid molecule; and

(d) detecting whether said nucleotide is methylated or not methylated

~~in~~ at said predetermined position in the sample wherein a methylated or a not methylated nucleotide is indicative of a pathological condition or the predisposed for said pathological condition.

13. (Original) The method of claim 12 wherein said pathological condition is cancer, a neurodegenerative disease or another neurological disorder.

14. (Original) The method of claim 13 wherein said cancer is a primary tumor, a metastasis or a residual tumor.

15. (Original) The method of claim 14 wherein said primary tumor is a glioma.

16. (Currently Amended) The method of claim 15 wherein said glioma is an astrocytoma, oligodendroglioma, an oligoastrocytoma, a glioblastoma, or a pilocytic astrocytoma.

17. (Original) The method of claim 13 wherein said neurodegenerative disease is Alzheimer's disease, Parkinson disease, Huntington disease, or Rett-Syndrome.

18. (Original) The method of claim 13 wherein said neurological disorder is Prader-Willi-Syndrom, Angelman-Syndrome, Fragile-X-Syndrome, or ATR-X-Syndrome.

19. (Previously Presented) The method of claim 12 wherein said nucleic acid molecule is a DNA molecule or an RNA molecule.

20. (Currently Amended) The method of claim 12 wherein ~~the amplification in step~~ in (b) the nucleic acid molecule is ~~effected by~~ amplified via LCR or PCR.

21. (Original) The method of claim 20 wherein one amplification primer is detectably labeled.

22. (Currently Amended) The method of claim 21 wherein said ~~label~~ amplification primer is labeled with (a) biotin, (b) avidin, (c) streptavidin or (d) a derivative of (a), (b or (c) or a magnetic bead.

23. (Previously Presented) The method of claim 12 wherein said methylated nucleotide is an adenine, guanine or a cytosine.

24. (Currently Amended) The method of claim 12 wherein said real-time sequencing comprises:

(a) hybridization of a sequencing primer to said amplified nucleic acid molecule in single-stranded form;

(b) addition of a DNA polymerase, a ATP sulfurylase a luciferase, an Apyrase, adenosine-phosphosulfate (APS) and luciferin;

(c) sequential addition of all four different dNTP's

(d) detection of a luminescent signal wherein the intensity of the luminescent signal is correlated with the incorporation of a specific nucleotide at a specific position in the nucleic acid molecule and wherein the intensity of said signal is indicative of the methylation status of said nucleotide ~~in~~ at said predetermined position.

25. (Previously Presented) The method of claim 12 further comprising quantifying the methylated nucleotides.

26. (Previously Presented) The method of claim 12 wherein said agent suitable for the conversion of said nucleotide to pair with a nucleotide normally not pairing with said nucleotide is a bisulfite, preferably sodium bisulfite.

27. (Previously Presented) The method of claim 1 wherein said method is a high-throughput method.

28. (New) The method of claim 12 wherein said sample is derived from tissue, a body fluid or stool.

29. (New) The method of claim 28 wherein said body fluid is blood, serum or urine.

30. (New) The method of claim 1 wherein said nucleotide is a cytosine and is part of one of the following sequences: CpG, CpNpG or CpNpN.

31. (New) The method of claim 1, wherein the methylation status of more than one predetermined nucleotide is detected and a number of samples are analyzed at the same time.

32. (New) A method for generating new nucleotide pairing partners upon amplification of at least one nucleic acid molecule for the detection of the methylation status of nucleotides of said nucleic acid molecule, said method comprising:

a. providing said at least one nucleic acid molecule;

b. treating said nucleic acid molecule with an agent suitable for conversion of a nucleotide if present in methylated form or non-methylated form to pair with nucleotide pairing partners normally not pairing with said nucleotide prior to conversion;

c. amplifying said nucleic acid molecule to produce an amplification product comprising said nucleotide pairing partners normally not pairing with said nucleotide prior to conversion;

d. real-time sequencing said amplification product;

e. determining the amount of said nucleotide pairing partner in said amplification product to detect the methylation status of nucleotides of said nucleic acid molecule.